CHARACTERISTICS OF AUTISM SPECTRUM DISORDER IN ANOREXIA NERVOSA: A NATURALISTIC STUDY IN AN INPATIENT TREATMENT PROGRAMME

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Abstract

Previous research has demonstrated links between Anorexia Nervosa (AN) and Autism Spectrum Disorder (ASD), however, few studies have examined the possible impact of symptoms of ASD on clinical outcomes in AN. The aim of this study was to examine the association between symptoms of ASD, eating disorder and other psychopathology during the course of inpatient treatment in individuals with AN. Participants with AN (n=171) completed questionnaires exploring eating disorder psychopathology, symptoms of depression and anxiety and everyday functioning at both admission and discharge. Characteristics associated with ASD were assessed using the AQ-10. ASD symptoms were significantly positively correlated with eating disorder psychopathology, work and social functioning and symptoms of depression and anxiety, but not with BMI. AQ-10 scores remained relatively stable from admission to discharge but there was a small, significant reduction in scores. There was no interaction between time and AQ-10 scores on clinical symptom change. In AN, ASD symptoms appear to be associated with a more severe clinical presentation on admission to inpatient care. ASD symptoms as assessed by self-report measures may be exacerbated by other mental health psychopathology, which warrants further investigation.

Keywords

Anorexia Nervosa; Autism Spectrum Disorder; ASD; AQ-10; eating disorder

Background

Anorexia Nervosa (AN) is an eating disorder characterized by deliberate weight loss; an intense fear of gaining weight and distorted body image (APA, 2013).The disorder is associated with high morbidity (Treasure et al., 2010) and mortality rates (Fichter and Quadflieg, 2016), as well as functional and social impairment (Tchanturia et al., 2013a; Harrison et al., 2014). Despite the high risks associated with the disorder, the evidence for successful treatment for AN in adults is limited (NICE, 2004). Challenges in treating severe AN include malnutrition, poor attention and inefficiencies in cognitive processing, which may limit patients' ability to benefit fully from psychological treatments (Tchanturia et al., 2011; Tchanturia et al., 2012b; Lang et al., 2014). Thus, over the last few years, treatment focus has started to shift from core eating disorder symptoms to other factors thought to maintain the disorder (Treasure and Schmidt, 2013).

Up to 97% of patients hospitalized for the treatment of AN experience at least one psychiatric co-morbidity (Blinder et al., 2006) making it an important factor to consider in treatment. Major Depressive Disorder is the most common comorbidity in AN (Kaye, 2008), and has been linked to a worse treatment outcome (Lowe et al., 2001). Generalized Anxiety Disorder (Godart et al., 2002; Kaye et al., 2004; Cederlof et al., 2015), has also been found to impede clinical outcomes of treatment. Possible co-morbidity between AN and Autism Spectrum Disorder (ASD) has received recent research attention, arising from observed similarities between the two disorders, with patients with AN showing inflexibility and poor social functioning, possibly reflecting the presence of an underlying ASD (Gillberg, 1983).

Both cognitive (Oldershaw et al., 2011; Tchanturia et al., 2012b; Westwood et al., 2016b) and socioemotional (Tchanturia et al., 2004; Nowakowski et al., 2013; Davies et al., 2016; Tchanturia et al., 2012a; Doris et al., 2014; Westwood et al., 2016a) similarities

between ASD and AN have been observed. Several studies have also explored the presence of elevated ASD symptoms in adults with AN (Huke et al., 2013; Westwood et al., 2015; Westwood et al., 2017b; Mandy and Tchanturia, 2015; Vagni et al., 2016; Bentz et al., 2017), suggesting that adults with AN exhibit higher levels of symptoms characteristic of ASD than the general population, with an estimated prevalence rate of around 23% (Huke et al., 2013; Westwood et al., 2017b). It is important to note that the presence of ASD symptoms in AN appears to differ across age groups and stages of the illness, suggesting that similarity between the two disorders may at least in part arise because of starvation or chronicity of AN. Thus, individuals with AN may only superficially resemble those with ASD (Mandy and Tchanturia, 2015; Westwood et al., 2017a; Bentz et al., 2017), rather than having a neurodevelopmental disorder. Examining the stability of ASD symptoms over the course of treatment for AN will speak to debates over whether behaviours characteristic of ASD are exaggerated, arising from the ill-state associated with AN (Hiller and Pellicano, 2013).

Research examining the effect of ASD symptoms on treatment outcome in AN has found a poorer prognosis when ASD symptoms are elevated (Nielsen et al., 2015; Stewart et al., 2017). Therefore, patients with AN and elevated symptoms of ASD may respond particularly poorly to standard treatment for AN (Goddard et al., 2013; Tchanturia et al., 2013b; Tchanturia et al., 2016). However, a small-scale pilot research suggested lower treatment drop-out in individuals with elevated ASD symptoms (Huke et al., 2014). Thus, more work is needed to clarify the clinical needs and necessary treatment adaptions for elevated ASD symptoms in AN. Better understanding of these symptoms could help improve service delivery and enable clinical teams to develop and enhance skills to provide tailored interventions.

The aim of this naturalistic study is to examine the association between symptoms of ASD and eating disorder and other psychopathology in patients with AN and to examine

whether changes in psychopathology during the course of inpatient treatment are dependent on ASD symptoms.

The specific research questions were as follows:

1. Is the level of self-reported symptoms of ASD associated with more severe eating disorder and other psychopathology at admission?
2. Are ASD symptoms stable over the course of inpatient admission?
3. Are changes in self-reported psychopathology and eating disorder symptoms associated with the severity of ASD symptoms?

Method

Participants

All participants, n=171, were part of an inpatient treatment programme at South London and Maudsley NHS Foundation Trust and had a DSM-5 diagnosis of AN (APA, 2013) on admission. Participants had a mean age of 27.3 years, mean age of AN onset of 16.18 years, a mean BMI of 14.1 on admission and an average length of treatment of 16 weeks. For a more detailed analysis of the participant's demographic information, see Table 1. As the sample was recruited from a clinical programme, there were no specific inclusion/exclusion criteria. All patients received a self-report questionnaire pack at admission and discharge.

Measures

Body Mass Index (BMI; kg/m^2) was taken from clinical notes on the day of the completion of the questionnaires on admission and discharge. Demographic variables were collected from participants and in case of missing data they were obtained from the clinical notes. Participants completed self-report questionnaires within a week of admission and no earlier than a week before discharge. The Hospital Anxiety and Depression Scale (HADS) was introduced to the audit questionnaire pack three years

later than the other measures and is hence reflected in the results as a lower response rate.

Autism-Spectrum Quotient, short version (AQ-10; Allison et al., 2012):

Participants completed the AQ-10 as part of their questionnaire packs on admission and discharge. The AQ-10 is a brief, ten-item, self-report questionnaire originally designed for use as a screening questionnaire for ASD. It shows equivalent validity to the longer version of the AQ (Booth et al., 2013), with a clinical cut-off of six indicating possible ASD. It has been used widely within eating disorder research to differentiate individuals with AN from healthy controls on level of ASD symptoms (Westwood et al., 2015). As the measure was designed as a screening tool and not a diagnostic measure, we treated the scores as a continuous variable with higher scores indicating an increase in autistic symptoms. This is also in line with the notion of ASD being a dimensional disorder (Wiggins et al., 2012), with sub-clinical symptoms extending into the general population.

Eating Disorder Examination Questionnaire (EDE-Q; Fairburn and Beglin, 1994):

A 36-item self-report measure looking at ED symptomatology and behaviours over the last 28 days. The questionnaire provides scores across four subscales (Dietary Restraint, Weight Concern, Shape Concern and Eating Concern) as well as a Global score, which reflects overall illness severity. In the current study, the overall Cronbach alpha coefficient was .98.

Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983):

A 14-item self-report questionnaire assessing presence and severity of depression and anxiety traits during the past week. The clinical cut off score is $\geq$10 for both depression and anxiety subscales, with a maximum possible score of 21. In the current study, the overall Cronbach alpha coefficient was .86.

Work and Social Adjustment Scale (WSAS; Mundt et al., 2002):

A 5-item self-report measure assessing the extent of impairment in the following domains: home management, ability to work, both social and private leisure, and ability to form and maintain close relationships. Each domain is scored on an 9-point Likert scale, ranging from 0 (no impairment) to 8 (very severe impairment). The maximum total score is 40, with a clinical cut off is 20 and above. In the current study, the overall Cronbach alpha coefficient was .85.

Data analysis:

All statistical analyses were conducted with Stata 14 (Stata Corp.). Significance threshold was set at $p < 0.05$. Additionally, effect size of change in psychopathology from admission to discharge was estimated by calculating standardized mean change with change score standardization. The effect size estimates were interpreted as small ($\geq |0.2|$), medium ($\geq |0.5|$), and large ($\geq |0.8|$) (Hedges, 1981).

Association between AQ-10 and eating disorder/other psychopathologies

The association between AQ-10 scores and eating disorder/other psychopathology was assessed using Kendall's tau-b (τ_b) correlation coefficient at admission to assess if those who score high on the AQ-10 come into hospital with other more severe psychopathology. The correlation analyses were corrected for multiple comparisons by adjusting the confidence intervals with the Bonferroni method.

Stability of AQ-10 scores over admission

AQ-10 scores were checked for stability over time by looking at the linear relationship between patients' admission and discharge scores using Kendall's tau-b. Secondly, Wilcoxon signed rank test was conducted to investigate significant changes in the AQ-10 score from admission to discharge.

Relationship between AQ-10 score and clinical symptom change

To investigate the association between AQ-10 scores and clinical symptom change over the course of admission, only participants who had completed questionnaires at admission are included. Drop-out rates were defined as non-completion of discharge questionnaires with common reasons being: not returning questionnaires, refusal to complete questionnaires, discharged prematurely and self-discharge from service. To allow the data to be analysed despite of drop-out, we conducted mixed effects analysis with time (admission, discharge) and AQ-10 scores as fixed effects predictors along with a random intercept. Any autocorrelation in the residuals was adjusted with the AR(1) autoregressor. All data met the assumptions for mixed effects analysis.

Results

Patient Characteristics

Self-reported psychopathology at admission and discharge is presented in Table 1. Based on the 95% confidence intervals, there were significant improvement in all measures of psychopathology and BMI with small to large effect sizes. All participants were female and were aged between 18 and 55 years with a mean age of onset of AN was 16.2 years (SD=6), leading to a mean illness duration of 10.8 years (SD=8.5). 58% percent of participants had restrictive AN, 33% had a diagnosis of AN binge-purge, and 9% had a diagnosis of atypical AN.

Table 1. Self-reported psychopathology and BMI at admission and discharge

	Admission		Discharge			95% CI	
Scale	Mean	SD	Mean	SD	SMCC	Lower bound	Upper bound
EDE-Q	3.85	1.66	2.80	1.65	-0.76	-0.99	-0.53

WSAS	26.54	8.85	20.95	10.71	-0.54	-0.76	-0.32
HADS anxiety	14.71	4.49	12.28	5.16	-0.40	-0.63	-0.16
HADS depression	11.73	4.98	7.53	5.05	-0.63	-0.88	-0.38
AQ-10	3.86	2.45	3.42	2.34	-0.27	-0.49	-0.06
BMI	14.15	1.66	16.31	1.90	1.51	1.29	1.74

EDE-Q = Eating disorder examination questionnaire; WSAS = Work and social adjustment scale; HADS = Hospital anxiety and depression scale; AQ-10 = Short autism-spectrum quotient; BMI = Body mass index; SMCC = standardized mean change with change score standardization; CI = confidence interval.

Association between AQ-10 and eating disorder/other psychopathology

Results of Kendall's tau-b correlation analysis, to determine the relationship between AQ-10 total score and other psychopathology scores at admission are displayed in Table 2. There was a significant positive correlation between AQ-10 and EDE-Q, WSAS, HADS Anxiety and HADS Depression, indicating that those reporting higher incidence of ASD symptoms also tend to report higher incidence of other psychopathology.

Table 2. Correlation between AQ-10 scores and psychopathology and BMI at admission

Scale	Correlation coefficient (τb)	p-value
EDE-Q	0.29	0.0001
WSAS	0.22	0.009
HADS: Anxiety	0.27	0.001

HADS: Depression	0.23	0.008
BMI	0.15	0.361

The confidence intervals were adjusted for multiple comparisons using the Bonferroni method. Significance was set at $p < 0.05$.

Stability of AQ-10 scores over time

The results of the Kendall's tau correlation show that there was a medium sized correlation between admission and discharge AQ-10 scores ($\tau b = 0.56, p < .001$), suggesting the scores are reasonably stable over time. There was, however, small decrease in AQ-10 scores between admission and discharge (SMCC = -0.27, 95% CI [-0.49, -0.06]), which was statistically significant (Z = 2.33, p = 0.020).

Relationship between AQ-10 scores and clinical symptom change of the course of admission

Depression

The mixed effects analysis showed that, as expected, there was a significant negative relationship between time and self-reported depression (Z = -2.88, p = 0.004, 95% CI [-5.00, -0.95]). There was also a significant positive relationship between AQ-10 scores and self-reported depression (Z = 4.01, p < 0.001, 95% CI [0.35, 1.01]). There was no significant time x AQ-10 interaction (Z = -0.27, p = 0.788, 95% CI [-0.57, 0.43]). These results indicate that the relationship between AQ-10 and self-reported depression was reasonably constant from admission to discharge with those reporting high incidence of ASD symptoms also reporting more depressive symptoms.

Anxiety

The mixed effects model revealed a significant positive relationship between AQ-10 scores and self-reported anxiety (Z = 4.12, p < 0.001, 95% CI [0.35, 0.98]). Surprisingly,

there was no significant negative relationship between time and self-reported anxiety (Z = -1.83, p = 0.067, 95% CI [-3.43, 0.12]). There was also no significant time x AQ-10 interaction (Z = -0.06, p = 0.953, 95% CI [-0.46, 0.43]). These results indicate that the relationship between AQ-10 scores and self-reported anxiety was reasonably constant from admission to discharge with those reporting high incidence of ASD symptoms also reporting more anxiety.

Eating Disorder Symptoms

As expected, the mixed effects analysis revealed a significant negative relationship between time and self-reported ED symptoms (Z = -3.05, p = 0.002, 95% CI [-1.25, -0.27]). There was also a positive relationship between AQ-10 scores and self-reported ED psychopathology such that those reporting more ED symptoms also reported more ASD symptoms (Z = 3.67, p < 0.001, 95% CI [0.08, 0.27]). There was no significant r time x AQ-10 interaction (Z = -0.72, p = 0.0.471, 95% CI [-0.16, 0.07]). These results suggest that the relationship between self-reported ASD and ED symptoms was reasonably constant from admission to discharge.

Body mass index (BMI)

The mixed effects model showed that there was a significant positive relationship between time and BMI (Z = 9.04, p < 0.001, 95% CI [2.00, 3.10]), as expected. Unlike with the above self-reported ED psychopathology, there was no significant relationship between AQ-10 scores and BMI (Z = 1.57, p = 0.116, 95% CI [-0.02, 0.18]). There was also no significant time x AQ-10 interaction (Z = -0.39, p = 0.697, 95% CI [-0.16, 0.10]).

Work and social adjustment

As anticipated, the mixed effects analysis showed a significant negative relationship between time and WSAS score (Z = -2.95, p = 0.003, 95% CI [-9.04, -1.82]). There was also a significant positive relationship between AQ-10 and WSAS scores (Z = 4.26, p <

0.001, 95% CI [0.68, 1.84]). There was no significant time x AQ-10 interaction (Z = 0.45, p = 0.655, 95% CI [-0.66, 1.04]). These results indicate that the relationship between AQ-10 and WSAS was reasonably constant across time with those reporting more ASD symptoms also report more difficulties in work and social adjustment.

Discussion

The aim of this naturalistic study was to explore the association between ASD symptoms and both eating disorder and other psychopathology and functioning in patients hospitalized for AN. The results indicate that symptoms of ASD, as measured by the AQ-10 are significantly, positively associated with both eating disorder and other psychopathology, as measured by the EDE-Q, WSAS, HADS Anxiety and HADS Depression. This suggests that individuals who report higher levels of symptoms associated with ASD also tend to report higher incidence of other psychopathology.

These results are in line with the few previous studies which have examined ASD symptoms in women with AN. For example, Westwood et al. (2017b) found that symptoms of ASD were associated with increased alexithymia and obsessive-compulsive symptoms. However, they did not find any association between symptoms of anxiety or depression or specific eating disorder pathology, including BMI. However, as Westwood and colleagues (2017b) used a direct-observational assessment of ASD, namely the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2; Lord et al., 2012), the results are not directly comparable. Interestingly, while in this study EDE-Q scores were significantly positively correlated with AQ-10 scores, BMI was not. This was also the case in both Westwood and colleagues studies with adults (2017b) and adolescents with AN (Westwood et al., 2017a). This could suggest that while ASD symptoms are associated with eating disorder psychopathology in AN, they are not associated with the physical symptoms accompanying the disorder, such as low body weight, malnutrition or starvation. This is contrary to previous suggestion that such physical symptoms could

exacerbate the relationship between AN and ASD (Hiller and Pellicano, 2013). While it is not possible to separate the physical and psychological consequences of AN, this is an area which would benefit from future research.

The second finding of this study was that while AQ-10 scores are relatively stable over the course of admission, there was a small yet significant reduction in these scores between admission and discharge. Given that ASD is a pervasive developmental disorder, developing during the early developmental period, with symptoms persisting into adulthood (NICE, 2012), one would not expect to see a reduction in such symptoms during an inpatient admission. This suggests that the AQ-10 may not just be measuring characteristics of ASD but may also be assessing symptoms associated with more general psychopathology, including symptoms of anxiety, depression or difficulties with general functioning.

This argument is supported by the finding here that all measures of psychopathology (EDE-Q, HADS, WSAS) were significantly positively correlated with the AQ-10. The AQ-10 focuses on current symptoms rather than assessing characteristics of ASD present earlier in life and despite being validated as a screening tool for use with adults (Booth et al., 2013), previous research has suggested that the AQ may not be .sensitive in detecting ASD in individuals with psychiatric disorders (Lugnegard et al., 2015). There is also evidence that scores on the AQ are less stable in females than in males (Whitehouse et al., 2011), although this study looked at individual scores over several years rather than a few months. Nevertheless, it might be that in individuals with severe AN, the AQ-10 is not sensitive enough to differentiate characteristics of ASD from other psychopathology, highlighting need for the development of brief, reliable tools for assessing ASD in psychiatric populations (Westwood and Tchanuria, 2017).

The mixed effect analysis showed that patient's self-report depression and eating disorder symptoms improved during the course of inpatient treatment. There was also a

signficiant increase in BMI and improvement in work and social functioning. While this was expected given the objectives of inpatient treatment, improvements in psychological symptoms, BMI and functioning were not influenced by or dependent on AQ-10 scores. However, individuals who reported higher levels of symptoms of ASD also reported higher levels of other clinical symptoms, irrespective of time. This suggests that while symptoms associated with ASD may not effect outcome, individuals with these symptoms may have more severe psychopathology in general compared with individuals without symptoms of ASD.

These findings support previous research suggesting pooer outcome in individuals with both AN and elevated symptoms of ASD (Stewart et al., 2017; Nielsen et al., 2015). In the study presented here, symptoms of ASD did not influence the outcome of inpatient treatment but individuals with such symptoms had more severe eatign disorder and depressive symptoms and poorer work and social functioning. This suggests that indivduals with charactersitics of ASD may require longer or more intensive treatment for AN, although it is not yet known whether such individuals would benefit from specifically tailored care pathways.

Interestingly, despite the effect size estimate showing a small, signficiant reduction in HADS anxirty scores from admission to discharge, when AQ-10 scores are included in the model as a predictor, there is no longer a signficiant reducion in HADs anxiety scores over time. There was no signficiant interaciton between time and AQ-10 scores for anxiety but there may be a relationship between HADS anxiety and the AQ-10 which was not detected within mediation analysis here. This oculd be due to statistical issues, i.e., using count (AQ-10) versus continuous (HADS anxiety) outcomes. However, the possible relationship between self-report depression and ASD symptom scores warrents further investigaiton.

Limitations

This study was based on naturalistic observations and therefore, the etiology or nature of the relationship between ASD symptoms and psychopathology cannot be inferred. While it is possible that the presence of ASD symptoms exacerbate symptoms of depression, anxiety and eating disorder pathology, the reverse may also be true, particularly as the AQ-10 measures current symptoms rather than assessing developmental history of ASD. Studies utilizing a longitudinal design, which assess ASD prior to the onset of AN will help delineate the relationship between these disorders.

The study was conducted in one, inpatient eating disorder service so is not widely generalizable. There is a possibility that individuals hospitalized for AN, at the more severe end of the eating disorder spectrum, are more likely to have elevated symptoms of ASD. The presence of ASD symptoms has been associated with greater need for treatment augmentation in adolescents (Stewart et al., 2017) and therefore such symptoms may be over-represented in adult inpatient samples.

Clinical implications

Both AN and ASD are difficult conditions to manage clinically, particularly given the high levels of co-morbidities apparent in both disorders (Russell et al., 2016; Blinder et al., 2006) and further research and developments are needed to tailor strategies to help individuals with both conditions (Anckarsater et al., 2012; Baron-Cohen et al., 2013; Tchanturia et al., 2016). In both ASD and AN, a gap in the literature has been acknowledged in terms of adult service provision (Howlin and Moss, 2012; Goddard et al., 2013) In AN, recent treatment developments have included adaptations to specific maintenance factors of the disorder. Cognitive Remediation Therapy (CRT) has been developed to address cognitive characteristics including cognitive inflexibility and detail-focused thinking (For a review, see Tchanturia et al., 2014). Cognitive Remediation and Emotion Skills Training (CREST) addresses poor recognition and

expression of emotions (Tchanturia et al., 2015) and the Maudsley Model of Anorexia Treatment for Adults (MANTRA; Schmidt et al., 2012) shows promise for patients with severe AN. Importantly, these treatments target the shared features between AN and ASD but further studies to assess their efficacy for individuals with both AN and elevated symptoms of ASD are needed.

Conclusion

The findings presented here suggest that in adults hospitalized for AN, the presence of symptoms characteristic of ASD is associated with more severe eating disorder, depression and anxiety symptoms and poorer everyday functioning. While the presence of ASD symptoms did not influence the outcome of admission directly, individuals with both AN and elevated symptoms of ASD may require longer or more intensive treatment packages.

Declarations

List of abbreviations:

AN = Anorexia Nervosa

AQ-10 = Autism Quotient, short version

ASD = Autism spectrum disorder

BMI = Body Mass Index

CI = confidence interval

CRT = Cognitive Remediation Therapy

CREST = Cognitive Remediation and Emotion Skills Training

EDE-Q = Eating disorders Examination Questionnaire

HADS = Hospital Anxiety and Depression Scale

MANTRA = the Maudsley Model of Anorexia Treatment for adults

SD = Standard Deviation

SMCC = standardized mean change with change score standardization

WSAS = Work and Social Adjustment Scale

Ethical approval and consent to participate

The National Research Ethics Service, Fulham, London (NRES-14/LO/2131) approved the study. All participants gave written, informed consent for their anonymized data to be used for research purposes.

Availability of data and materials

Available upon request.

Competing interests

N/A

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Authors Contributions

KT conceived and designed the study, coordinated and helped to draft the manuscript. JA contributed to data collection and preparation of the manuscript. JL completed the statistical analyses and helped to draft the manuscript. All authors approved the final manuscript. HW helped design the study and prepare the manuscript.

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